

Appl. No. 10/798,639

Reply dated April 18, 2006

Reply to Office Action mailed October 19, 2006

1. Amendments to the Claims:

1. (Currently Amended) A device for performing chemical reactions, comprising a substrate having a first side, and a second side opposite the first side and an array of microwells formed in the substrate, each microwell comprising a porous region: (a) defined by a continuous portion of the substrate; (b) capable of binding sample molecules; (b) defined in the first side of the substrate; (c) formed by selective removal of a substrate constituent; and (d) extending partially through the substrate.

2. (Previously Presented) The device of claim 1, wherein each microwell holds a sample such that a liquid sample in one microwell does not intermix with a liquid sample from another microwell.

3. (Currently Amended) The device of claim 1, wherein pores within the porous region are at least 2.5 to 32 nanometers in size.

4. (Currently Amended) The device of claim 1, wherein pores within the porous region are between 7.5 and 32.0 ~~60.0~~ nanometers in size.

5. (Previously Presented) The device of claim 1, wherein the substrate is a borosilicate glass.

6. (Previously Presented) The device of claim 5, wherein the porous region is formed by heating the substrate, thereby causing ion constituent of the substrate to coalesce, and removing coalesced constituent by chemical dissolution.

7. (Previously Presented) The device of claim 1, further comprising a cavity located on the second side of the substrate and extending partially through the substrate to intersect the porous region.

8. (Previously Presented) The device of claim 7, wherein the porous region and the cavity are aligned such that the microwell forms a continuous channel extending through the substrate.

9. (Currently Amended) The device of claim 7, wherein at least a portion ~~portion~~ of the microwell further comprises a reactive monolayer deposited thereon.

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10. (Previously Presented) The device of claim 9, wherein the reactive monolayer comprises a plurality of organothiol molecules covalently bonded to a metallic layer.

11. (Previously Presented) The device of claim 10, wherein the organothiol molecules are alkylthiols.

12. (Previously Presented) The device of claim 10, wherein the metallic layer comprises gold.

13. (Previously Presented) The device of claim 7, further comprising an electrode coupled with at least one microwell.

14. (Previously Presented) The device of claim 13, wherein the electrode is positioned in the cavity.

15. (Previously Presented) The device of claim 14, wherein the electrode is capable of applying an electrical stimulus to the porous region of the microwell with which the electrode is coupled.

16. (Previously Presented) The device of claim 15, wherein electrode comprises a material selected from the group consisting of aluminum, gold, silver, tin, copper, platinum, palladium, carbon, and semiconductor materials.

17. (Previously Presented) The device of claim 8, wherein each microwell is capable of forming an ion bridge between the two sides of the substrate.

18. (Previously Presented) The device of claim 17, further comprising a conductive material deposited in the cavity.

19. (Previously Presented) The device of claim 18, wherein the conductive material comprises a conductive epoxy, electroless nickel plating, conductive gel, or conductive polymer.

20. (Previously Presented) The device of claim 1, further comprising a sample containment layer deposited on the first side such that a sample present in one microwell does not intermix with a sample present in another microwell.

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21. (Previously Presented) The device of claim 20, wherein the sample containment layer is hydrophobic.

22. (Previously Presented) The device of claim 20, wherein the sample containment layer is hydrophilic.

23. (Previously Presented) The device of claim 1, further comprising a marker that conveys information about the location of the microwells on the substrate.

24. (Previously Presented) The device of claim 23, wherein the marker is a bar code.

25. (Previously Presented) The device of claim 23, wherein the marker comprises a series of alternating reflective and non-reflective surfaces.

26. (Previously Presented) The device of claim 1, further comprising a means for conveying information about the location of the microwells on the substrate.

27. (Previously Presented) A device for performing chemical reactions comprising a substrate having an array of microwells, each microwell comprising: (a) a porous region, formed in a first side of the substrate capable of binding sample molecules, wherein the porous region is a continuous portion of the substrate, extends partially through the substrate, and is formed by selectively removing at least one constituent of the substrate; and (b) a cavity located at a side of the substrate opposite the first side and extending partially through the substrate to intersect the porous region.

28. (Previously Presented) The device of claim 27, wherein each microwell holds a sample such that a liquid sample in one microwell does not intermix with a liquid sample from another microwell.

29. (Currently Amended) The device of claim 27, wherein pores within the porous region are at least 2.5 to 32 nanometers in size.

30. (Currently Amended) The device of claim 27, wherein pores within the porous region are between 7.5 and 32.0 ~~60.0~~ nanometers in size.

31. (Previously Presented) The device of claim 27, wherein the substrate is a borosilicate glass.

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32. (Previously Presented) The device of claim 31, wherein the porous region is formed by heating the substrate, thereby causing ion constituent of the substrate to coalesce, and removing coalesced constituent by chemical dissolution.

33. (Previously Presented) The device of claim 27, wherein the porous region and the cavity are aligned such that the microwell forms a continuous channel extending through the substrate.

34. (Currently Amended) The device of claim 27, wherein at least a portion ~~portion~~ of the microwell further comprises a reactive monolayer deposited thereon.

35. (Previously Presented) The device of claim 34, wherein the reactive monolayer comprises a plurality of organothiol molecules covalently bonded to a metallic layer.

36. (Previously Presented) The device of claim 35, wherein the organothiol molecules are alkylthiols.

37. (Previously Presented) The device of claim 35, wherein the metallic layer comprises gold.

38. (Previously Presented) The device of claim 27, further comprising an electrode coupled with at least one microwell.

39. (Previously Presented) The device of claim 38, wherein the electrode is positioned in the cavity.

40. (Previously Presented) The device of claim 39, wherein the electrode is capable of applying an electrical stimulus to the porous region of each microwell with which the electrode is coupled.

41. (Previously Presented) The device of claim 40, wherein electrode comprises a material selected from the group consisting of aluminum, gold, silver, tin, copper, platinum, palladium, carbon, and semiconductor materials.

42. (Previously Presented) The device of claim 33, wherein the microwell capable of forming an ion bridge between two sides of the substrate.

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43. (Previously Presented) The device of claim 42, further comprising a conductive material deposited in the cavity.

44. (Previously Presented) The device of claim 43, wherein the conductive material comprises a conductive epoxy, electroless nickel plating, conductive gel, or conductive polymer.

45. (Previously Presented) The device of claim 27, further comprising a sample containment layer deposited on the first side such that a sample present in one microwell does not intermix with a sample present in another microwell.

46. (Previously Presented) The device of claim 45, wherein the sample containment layer is hydrophobic.

47. (Previously Presented) The device of claim 45, wherein the sample containment layer is hydrophilic.

48. (Previously Presented) The device of claim 27, further comprising a marker that conveys information about the location of the microwells on the substrate.

49. (Previously Presented) The device of claim 48, wherein the marker is a bar code.

50. (Previously Presented) The device of claim 48, wherein the marker comprises a series of alternating reflective and non-reflective surfaces.

51. (Previously Presented) The device of claim 27, further comprising at least one component of a chemical reaction to be carried out in the device.

52. (Previously Presented) The device of claim 51, wherein component is immobilized to the porous region.

53. (Previously Presented) The device of claim 51, wherein the component is a reagent used in a oligonucleotide synthesis reaction.

54. (Previously Presented) The device of claim 53, wherein the reagent is a nucleic acid.

55. (Withdrawn) A method of producing a device for performing an array of chemical reactions, the method comprising: providing a substrate having a first side and a second side, and forming an array of microwells in the substrate, wherein the microwells are formed by: (a)

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selectively leaching defined areas on the first side of the substrate, thereby forming a plurality of porous regions that are a continuous portion of the substrate and extend partially through the substrate; and (b) selectively etching defined areas of the second side of the substrate, thereby forming a plurality of cavities, wherein each cavity extends partially through the substrate to intersect with a porous region.

56. (Withdrawn) The method of 55, wherein the substrate is borosilicate glass.

57. (Withdrawn) The method of 55, wherein selectively leaching includes the steps of applying a mask to the first side of the substrate and contacting the first side with a leachant.

58. (Withdrawn) The method of 55, wherein selectively etching includes the steps of applying a mask to the second side of the substrate and contacting the second side with an etchant.

59. (Withdrawn) The method of 55, further comprising contacting the porous region with an etchant, thereby increasing pore size in the porous region.

60. (Withdrawn) The method of 55, further comprising immobilizing a sample molecule in the porous region.

61. (Withdrawn) A method of simultaneously conducting a plurality of chemical reactions, the method comprising: (a) providing a substrate having an array of microwells, each microwell comprising: (1) a porous region, formed in a first side of the substrate capable of binding sample molecules, wherein the porous region is a continuous portion of the substrate, extends partially through the substrate, and is formed by selectively removing at least one constituent of the substrate; (2) a cavity located at a side of the substrate opposite the first side and extending partially through the substrate to intersect the porous region; (b) introducing, under suitable reaction conditions, a plurality of test samples into a plurality of microwells of the substrate, wherein the test samples contain necessary reaction components, thereby conducting a plurality of chemical reactions.

62. (Withdrawn) The method of 61, wherein the chemical reactions are selected from the group consisting of ligation reactions, primer extension reactions, nucleotide sequencing

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reactions, restriction endonuclease digestions, biological interactions, oligonucleotide synthesis reactions, and polynucleotide hybridization reactions.

63. (Withdrawn) The method of 62, wherein the biological interactions are avidin-biotin interactions, antigen-antibody interactions, enzyme-substrate reactions, ligand-receptor interactions.

64. (Withdrawn) The method of 61, wherein the chemical reaction is a phosphoramidite chemical reaction for oligonucleotide synthesis.

65. (Withdrawn) The method of 61, wherein the test samples are immobilized to the porous region of a microwell.

66. (Withdrawn) A method of detecting an analyte in a plurality of test samples, the method comprising: (a) contacting each test sample in a plurality of test samples with a microwell defined a substrate having an array of microwells, each microwell comprising: (1) a porous region, formed in a first side of the substrate capable of binding sample molecules, wherein the porous region is a continuous portion of the substrate, extends partially through the substrate, and is formed by selectively removing at least one constituent of the substrate; (2) a cavity located at a side of the substrate opposite the first side and extending partially through the substrate to intersect the porous region; and (3) a probe immobilized to the porous region; (b) forming a complex between the probe and the analyte; and (c) detecting, in each microwell contacted with a test sample, the probe-analyte complex, thereby detecting the analyte in a plurality of test samples.

67. (Withdrawn) The method of claim 66, wherein the test sample is a bodily fluid, a suspension of solids in an aqueous solution, a cell extract, or a tissue homogenate.

68. (Withdrawn) The method of claim 67, wherein the bodily fluid is selected from urine, blood, plasma, serum, saliva, semen, stool, sputum, cerebral spinal fluid, tears, or mucus.

69. (Withdrawn) The method of claim 66, wherein the probe is selected from small molecules, organic functional groups, biomolecules, metals, metal chelates, and organometallic compounds.

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70. (Withdrawn) The method of claim 69, wherein the probe is a biomolecule selected from a protein polynucleotide, peptide, antibody, or fragment thereof.

71. (Withdrawn) A method of assembling a plurality of compounds, comprising: (a) providing a substrate having an array of microwells, each microwell comprising: (1) a porous region, formed in a first side of the substrate capable of binding sample molecules, wherein the porous region is a continuous portion of the substrate, extends partially through the substrate, and is formed by selectively removing at least one constituent of the substrate; (2) a cavity located at a side of the substrate opposite the first side and extending partially through the substrate to intersect the porous region; (b) adding a first component of the compound to a plurality of microwells, such that the first component binds to each porous region of the microwells; (c) adding a second component of the compound to the microwells; and (d) reacting the first component and second component to form a product in each of the plurality of microwells, thereby assembling a plurality of compounds.

72. (Withdrawn) The claim of 71, further comprising the steps of adding an additional component of the compound to the microwells and reacting the additional component of the compound with the product.

73. (Withdrawn) The claim of 72, further comprising repeating the steps of G2 to produce a compound of the desired length.

74. (Withdrawn) The method of claim 71, wherein the compound is a peptide or a oligonucleotide.

75. (Withdrawn) The method of claim 71, wherein the components of the compound are amino acids or nucleic acids.

76. (Withdrawn) The method of claim 71, wherein the product is a polypeptide or oligonucleotide.

77. (Withdrawn) A kit comprising a device for performing chemical reactions, the device comprising a substrate having an array of microwells, each microwell having: (a) a porous region formed in a first side of the substrate and capable of binding sample molecules, wherein the



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porous region is a continuous portion of the substrate, extends partially through the substrate, and is formed by selectively removing at least one constituent of the substrate; and (b) a cavity located at a side of the substrate opposite the first side and extending partially through the substrate to intersect the porous region; and further comprising a reaction component packaged in a suitable container.

78. (Withdrawn) The kit of claim 77, wherein the reaction component is a reagent for performing a reaction selected from the group consisting of ligation reactions, primer extension reactions, nucleotide sequencing reactions, restriction endonuclease digestions, oligonucleotide synthesis, hybridization reactions and biomolecular interactions.

79. (Withdrawn) The device of claim 77, wherein the substrate is a borosilicate glass.

80. (Withdrawn) The device of claim 77, further comprising an electrode coupled with at least one microwell and capable of applying an electrical stimulus to the porous region of the microwell with which the electrode is coupled.

81. (Withdrawn) The device of claim 77, further comprising a sample containment layer deposited on the first side such that a sample present in one microwell does not intermix with a sample present in another microwell.

82. (Withdrawn) The device of claim 77, further comprising a marker conveying information about the location of the microwells on the substrate.

83. (New). A device for performing chemical reactions, comprising a borosilicate glass substrate and an array of microwells formed in the borosilicate glass substrate, each microwell comprising a porous region, extending partially through the substrate, that is formed by selective removal of boron ions from the borosilicate glass substrate to leave voids in the borosilicate glass substrate wherein sample molecules can bind to the voids in the borosilicate glass substrate.

84. (New) The device of claim 83, wherein the porous region is formed by leaching the boron ions from the borosilicate glass substrate.